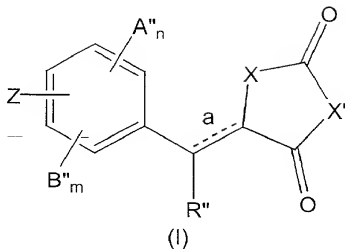
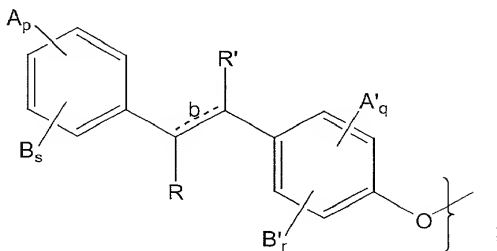


What is claimed is:

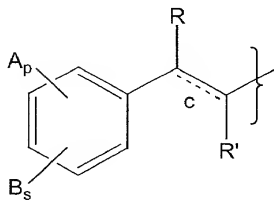
1. A compound of a formula I:



wherein Z is



H; A''; B''; or



- 5 n, m, q and r are independently integers from zero to 4 provided that  $n + m \leq 4$  and  $q + r \leq 4$ ; p and s are independently integers from zero to 5 provided that  $p + s \leq 5$ ; a, b and c are double bonds which may be present or absent;

when present; the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

R, R' and R'' are independently H, C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl, C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, -CO<sub>2</sub>Z', wherein Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium, ammonium, tromethamine, and the like; -CO<sub>2</sub>R''', -NH<sub>2</sub>, -NHR''', -NR<sub>2</sub>'', -OH, -OR''', halo, substituted C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or substituted C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, wherein R''' is C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or linear or branched alkenyl;

A, A' and A'' are independently H, C<sub>1</sub>-C<sub>20</sub> acylamino;

C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;

C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl; C<sub>1</sub>-C<sub>20</sub> alkoxy;

C<sub>1</sub>-C<sub>20</sub> alkylamino; C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; carboxyl; cyano; halo; hydroxy;

B, B' and B'' are independently H;

C<sub>1</sub>-C<sub>20</sub> acylamino; C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;

C<sub>1</sub>-C<sub>20</sub> alkenoyl; C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl;

C<sub>1</sub>-C<sub>20</sub> alkoxy; C<sub>1</sub>-C<sub>20</sub> alkylamino;

C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; aroyl, aralkanoyl; carboxyl; cyano; halo;

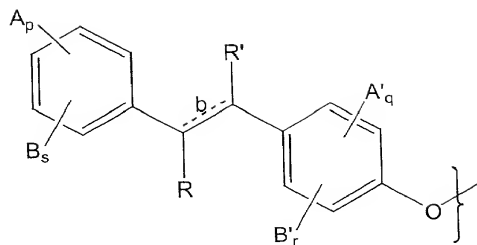
hydroxy;

or A and B together, or A' and B' together, or A'' and B'' together, may be

joined to form a methylenedioxy or ethylenedioxy group; and

X, X' are independently -NH-, -NR''', O or S.

2. A compound according to claim 1, wherein Z is

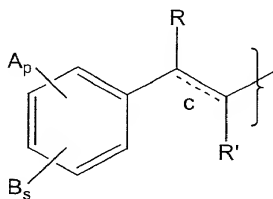


3. A compound according to claim 1, wherein Z is hydrogen.

4. A compound according to claim 1, wherein Z is A''.

5. A compound according to claim 1, wherein Z is B''.

6. A compound according to claim 1, wherein Z is

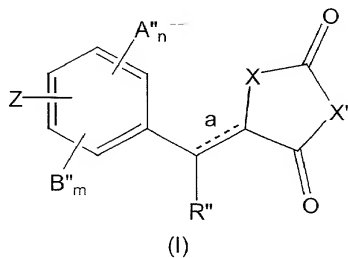


7. A compound according to claim 2, wherein X is sulfur, X' is -NH;  
A''<sub>n</sub>, B'', B', A<sub>p</sub>, A'<sub>q</sub>, R and R'' are all hydrogen.

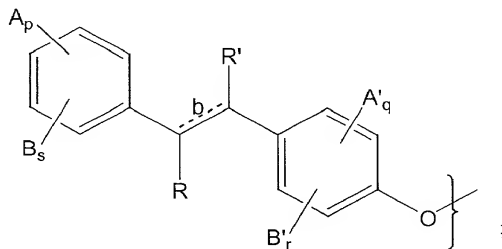
8. A compound according to claim 7, wherein B is methoxy, s is 2 and  
R' is carbomethoxy.

9. A compound according to claim 8, which is 5-(4-(1-carbomethoxy-2-(3,5-dimethoxy phenyl) ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.

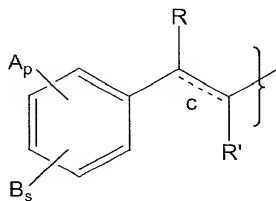
- 5 10. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula I:



wherein Z is



H; A''; B''; or



n, m, q and r are independently integers from zero to 4 provided that  $n + m \leq 4$  and  $q + r \leq 4$ ; p and s are independently integers from zero to 5 provided that  $p + s \leq 5$ ; a, b and c are double bonds which may be present or absent; when present, the double bonds may be in the E or Z configuration and, when  
5 absent, the resulting stereocenters may have the R- or S- configuration;

R, R' and R'' are independently H, C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl, C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, -CO<sub>2</sub>Z', where Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium,  
10 ammonium, tromethamine, and the like; -CO<sub>2</sub>R''', -NH<sub>2</sub>, -NHR''', -NR<sub>2</sub>'', -OH, -OR''', halo, substituted C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or substituted C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, wherein R''' is C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or linear or branched alkenyl;

15 A, A' and A'' are independently H, C<sub>1</sub>-C<sub>20</sub> acylamino;  
C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;  
C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl; C<sub>1</sub>-C<sub>20</sub> alkoxy;  
C<sub>1</sub>-C<sub>20</sub> alkylamino; C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; carboxyl; cyano;  
halo; hydroxy;

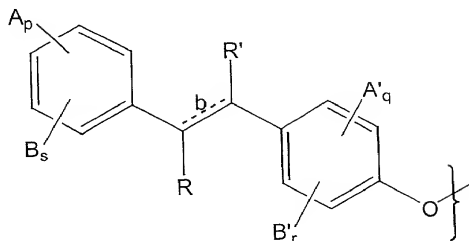
20 B, B' and B'' are independently H;  
C<sub>1</sub>-C<sub>20</sub> acylamino; C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;  
C<sub>1</sub>-C<sub>20</sub> alkenoyl; C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl;  
C<sub>1</sub>-C<sub>20</sub> alkoxy; C<sub>1</sub>-C<sub>20</sub> alkylamino;  
25 C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; aroyl, aralkanoyl; carboxyl; cyano; halo;  
hydroxy;

or A and B together, or A' and B' together, or A'' and B'' together, may be joined to form a methylenedioxy or ethylenedioxy group; and

X, X' are independently -NH, -NR''', O or S.

30 in a physiologically acceptable carrier.

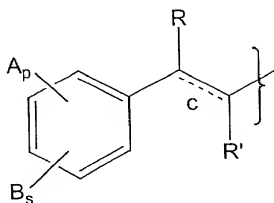
11. A composition according to claim 10, wherein Z is



12. A composition according to claim 10, wherein Z is A''.

13. A composition according to claim 10, wherein Z is B''.

14. A composition according to claim 10, wherein Z is

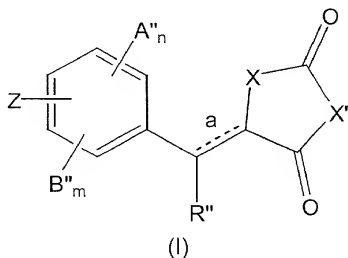


15. A composition according to claim 10, wherein X is sulfur, X' is -NH and A'', B'', A'\_q, B', A\_p, R and R'' are all hydrogen.

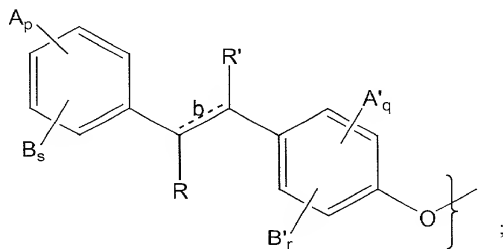
16. A composition according to claim 15, wherein R' is carbomethoxy; B is methoxy and s is 2.

17. A composition according to claim 16, wherein said compound is 5-(4-(4-(1-carbomethoxy-2-(3,5 dimethoxy phenyl) ethenyl) -phenoxy)-benzyl)-2,4-thiazolidinedione.

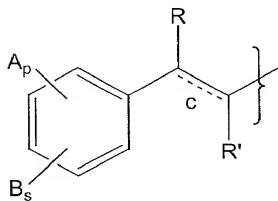
- 5 18. A method of treating diabetes comprising the steps of administering to a subject suffering from a diabetic condition, a therapeutically effective amount of a compound according to the formula I:



wherein Z is



H; A''; B''; or



n, m, q and r are independently integers from zero to 4 provided that  $n + m \leq 4$  and  $q + r \leq 4$ ; p and s are independently integers from zero to 5 provided that  $p + s \leq 5$ ; a, b and c are double bonds which may be present or absent; when present, the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

- 10 R, R' and R'' are independently H, C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl, C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, -CO<sub>2</sub>Z', where Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium, ammonium, tromethamine, and the like; -CO<sub>2</sub>R''', -NH<sub>2</sub>, -NHR''', -NR<sub>2</sub>'', -OH, -OR''', halo, substituted C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or substituted C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, wherein R''' is C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or linear or branched alkenyl;
- 15

A, A' and A'' are independently H, C<sub>1</sub>-C<sub>20</sub> acylamino;

C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;

- 20 C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl; C<sub>1</sub>-C<sub>20</sub> alkoxy;

C<sub>1</sub>-C<sub>20</sub> alkylamino; C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; carboxyl; cyano;

halo; hydroxy;

B, B' and B'' are independently H;

- 25 C<sub>1</sub>-C<sub>20</sub> acylamino; C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;

C<sub>1</sub>-C<sub>20</sub> alkenoyl; C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl;

C<sub>1</sub>-C<sub>20</sub> alkoxy; C<sub>1</sub>-C<sub>20</sub> alkylamino;

C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; aroyl, aralkanoyl; carboxyl; cyano; halo;

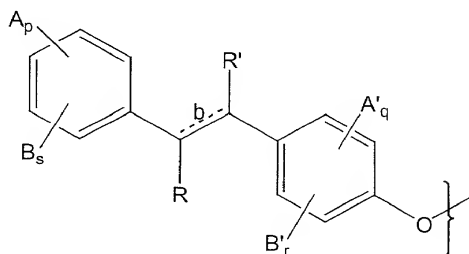
hydroxy;



or A and B together, or A' and B' together, or A'' and B'' together, may be joined to form a methylenedioxy or ethylenedioxy group; and X, X' are independently -NH, -NR''', O or S, in a physiologically acceptable carrier.

5

19. A method according to claim 18, wherein Z is



20. A method according to claim 19, wherein Z is H.

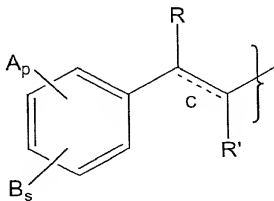
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21. A method according to claim 18, wherein Z is A''.

22. A method according to claim 18, wherein Z is B''.

15

23. A method according to claim 18, wherein Z is



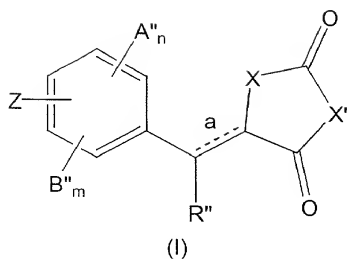
24. A method according to claim 18, wherein R'', A'', B'', A'q, B', Ap and R are all hydrogen, X is sulfur and X' is NH.

25. A method according to claim 18, wherein R'' is carbomethoxy  
5 and B is methoxy and s is 2.

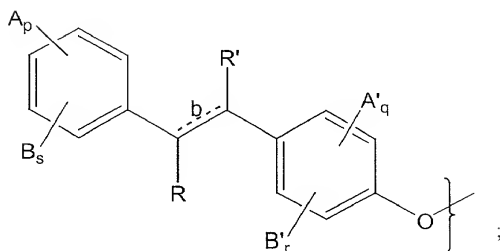
26. A method according to claim 18, wherein said compound is 5-(4-(4-(1-carbomethoxy-2-,3,5-dimethoxy phenyl) ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.

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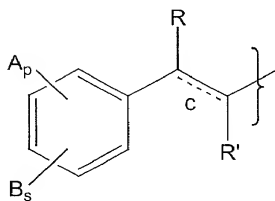
27. A method of treating inflammation comprising the steps of administering to a subject suffering from an inflammatory condition, a therapeutically effective amount of a compound according to the formula I:



wherein Z is



H; A''; B''; or



- 5 n, m, q and r are independently integers from zero to 4 provided that  $n + m \leq 4$  and  $q + r \leq 4$ ; p and s are independently integers from zero to 5 provided that  $p + s \leq 5$ ; a, b and c are double bonds which may be present or absent; when present, the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

R, R' and R'' are independently H, C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl, C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, -CO<sub>2</sub>Z', where Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium, ammonium, tromethamine, and the like; -CO<sub>2</sub>R''', -NH<sub>2</sub>, -NHR''', -NR<sub>2</sub>'', -OH, -OR''', halo, substituted C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or substituted C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, wherein R''' is C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or linear or branched alkenyl;

A, A' and A'' are independently H, C<sub>1</sub>-C<sub>20</sub> acylamino;

C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;

C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl; C<sub>1</sub>-C<sub>20</sub> alkoxy;

C<sub>1</sub>-C<sub>20</sub> alkylamino; C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; carboxyl; cyano;

halo; hydroxy;

B, B' and B'' are independently H;

C<sub>1</sub>-C<sub>20</sub> acylamino; C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;

C<sub>1</sub>-C<sub>20</sub> alkenoyl; C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl;

C<sub>1</sub>-C<sub>20</sub> alkoxy; C<sub>1</sub>-C<sub>20</sub> alkylamino;

C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; aroyl, aralkanoyl; carboxyl; cyano; halo;

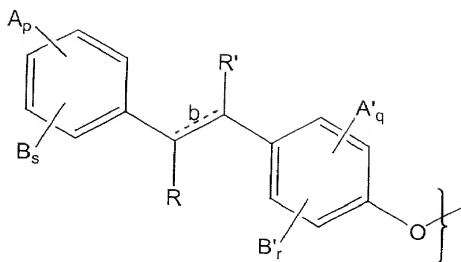
hydroxy;

or A and B together, or A' and B' together, or A'' and B'' together, may be joined to form a methylenedioxy or ethylenedioxy group; and

X, X' are independently -NH, -NR''', O or S,

in a physiologically acceptable carrier.

28. A method according to claim 27, wherein Z is

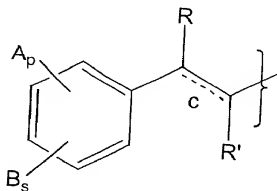


29. A method according to claim 27, wherein Z is H.

30. A method according to claim 27, wherein Z is A''.

31. A method according to claim 27, wherein Z is B''.

32. A method according to claim 27, wherein Z is

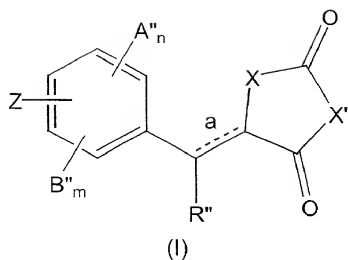


33. A method according to claim 27, wherein R'', A'', B'', A'\_q, B', A\_p and R are all hydrogen, X is sulfur and X' is NH.

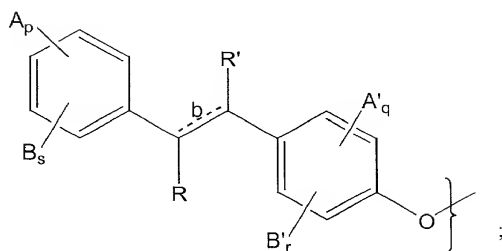
34. A method according to claim 33, wherein R' is carbomethoxy and B is methoxy and s is 2.

35. A method according to claim 27, wherein said compound is 5-(4-(4-(1-carbomethoxy-2-)3,5-dimethoxy phenyl) ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.

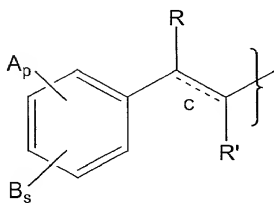
5 36. A method of treating immunological disease comprising the steps of administering to a subject suffering from an immunological disease, a therapeutically effective amount of a compound according to the formula I:



wherein Z is



H; A''; B''; or



$n$ ,  $m$ ,  $q$  and  $r$  are independently integers from zero to 4 provided that  $n + m \leq 4$  and  $q + r \leq 4$ ;  $p$  and  $s$  are independently integers from zero to 5 provided that  $p + s \leq 5$ ;  $a$ ,  $b$  and  $c$  are double bonds which may be present or absent;

- 5 when present, the double bonds may be in the E or Z configuration and when absent, the resulting stereocenters may have the R- or S- configuration;

R, R' and R'' are independently H, C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl, C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, -CO<sub>2</sub>Z', where Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium, ammonium, tromethamine, and the like; -CO<sub>2</sub>R''', -NH<sub>2</sub>, -NHR''', -NR<sub>2</sub>'', -OH, -OR''', halo, substituted C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or substituted C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, wherein R''' is C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or linear or branched alkenyl;

A, A' and A'' are independently H, C<sub>1</sub>-C<sub>20</sub> acylamino;

C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;  
C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl; C<sub>1</sub>-C<sub>20</sub> alkoxy;  
C<sub>1</sub>-C<sub>20</sub> alkylamino; C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; carboxyl; cyano;  
halo; hydroxy;

B, B' and B'' are independently H;

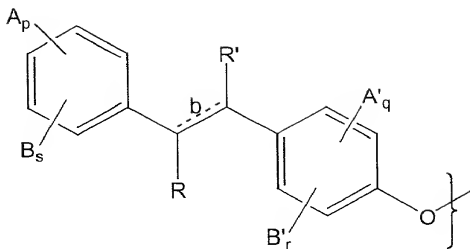
C<sub>1</sub>-C<sub>20</sub> acylamino; C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;  
C<sub>1</sub>-C<sub>20</sub> alkenoyl; C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl;  
C<sub>1</sub>-C<sub>20</sub> alkoxy; C<sub>1</sub>-C<sub>20</sub> alkylamino;  
C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; aroyl, aralkanoyl; carboxyl; cyano; halo;  
hydroxy;

or A and B together, or A' and B' together, or A'' and B'' together, may be joined to form a methylenedioxy or ethylenedioxy group; and

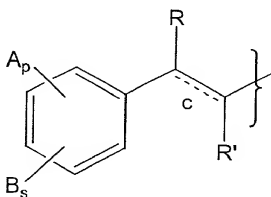
X, X' are independently -NH, -NR''', O or S,  
in a physiologically acceptable carrier.

37. A method according to claim 36, wherein Z is





38. A method according to claim 36, wherein Z is H.
39. A method according to claim 36, wherein Z is A''.
40. A method according to claim 36, wherein Z is B''.
41. A method according to claim 36, wherein Z is



42. A method according to claim 36, wherein R'', A'', B'', A'\_q, B', A\_p and R are all hydrogen, X is sulfur and X' is NH.
43. A method according to claim 42, wherein R' is carbomethoxy and B is methoxy and s is 2.

44. A method according to claim 36, wherein said compound is 5-(4-(4-(1-carbomethoxy-2-)3,5-dimethoxy phenyl) ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.

45. A method of inhibiting the activity of TNF-alpha, IL-1, IL-6 or COX-2 which comprises administering to a host in need of such inhibition an effective amount of a compound according to claim 1.

46. The method of treating inflammation, inflammatory or immunological disease which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

47. The method of inhibiting the undesired action of cytokine or cyclooxygenase which comprises administering to a host in need of such inhibition an effective amount of a compound according to claim 1.

48. The method of treating an inflammatory disease mediated by cytokines or cyclooxygenase which comprises administering to a host in need of such treatment a compound according to claim 1.

49. The method of treating insulin resistance which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

50. The method of treating hyperlipidemia which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

51. The method of treating coronary heart disease which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

52. The method of treating multiple sclerosis which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

53. The method of treating cancer which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

54. The method of claim 45, 46, 47, 48, 49, 50, 51, 52 or 53 wherein the compound is 5-(4-(4-(1-carbomethoxy)-2-(3,5-dimethoxyphenyl)-ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.

55. A compound according to claim 1 selected from the group consisting of:

3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N,N-dimethyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N-methoxy,-N-methyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-propionic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-acrylic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-propionic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-propionic acid,



together with a physiologically acceptable carrier therefor.

58. The pharmaceutical composition of claim 57 wherein said compound is 3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl]-acrylic acid.

59. The method of claim 18, 45, 46, 47, 48, 49, 50, 51, 52 or 53 wherein said compound is selected from the group consisting of

3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl]-acrylic acid,

3-(3,5-dimethoxy-phenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl]-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl]-N,N-dimethyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl]-N-methoxy,-N-methyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl]-propionic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl]-acrylic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl]-propionic acid,

3-(3,5-dimethoxy-phenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl]-propionic acid,

3-(3,5-dimethoxy-phenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl]-acrylic acid, and

3-(3,5-dimethoxy-phenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl]-propionic acid methyl ester.

60. The method of claim 59 wherein the compound is 3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl]-acrylic acid.

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